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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/731,366	12/06/2000	Joshua S. Salafsky	0575/60934/JPW/ADM	8346

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EXAMINER
COUNTS, GARY W

ART UNIT	PAPER NUMBER
1641	

DATE MAILED: 02/07/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Appli ant(s)	
	09/731,366	SALAFSKY ET AL.	
	Examiner	Art Unit	
	Gary W. Counts	1641	

-- Th MAILING DATE of this communication appears on th cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 October, 2001* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-32* is/are pending in the application.

4a) Of the above claim(s) *29-32* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-28* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Election/Restrictions

Applicant's election with traverse of Group I, claims 1-28 in Paper No. 7 is acknowledged. The traversal is on the ground(s) that Group I and Group II are not independent and that there would not be a serious burden on the examiner if restriction were not required. This is not found persuasive because the search for group II requires different search terms and a different search strategy which creates a burden on the examiner. The record set forth in the previous restriction requirement clearly indicated that the delineated inventions are in fact patentably distinct each from the other or independent from the other. The requirement is still deemed proper and is therefore made **FINAL** for reasons of record.

Information Disclosure Statement

The listing of references in the specification is not a proper information disclosure statement. 37 CFR 1.98(b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP § 609 A(1) states, "the list may not be incorporated into the specification but must be submitted in a separate paper." Therefore, unless the references have been cited by the examiner on form PTO-892, they have not been considered.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by th inventor of carrying out his invention.

Claims 1-28 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for amine-specific dyes and sulfhydryl-specific dyes, does not reasonably provide enablement for all second harmonic-active moieties. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Enablement requires that the specification teach those in the art to make and use the invention without undue experimentation. The factors that must be considered in determining undue experimentation are set forth in *In re W*ands USPTQ2d 14000. Factors to be considered in determining whether a disclosure would require undue experimentation include (1) the nature of the invention, (2) the state of the prior art, (3) the predictability or lack thereof in the art, (4) the amount of direction or guidance present, (5) the presence or absence of working examples, (6) the quantity of experimentation necessary, (7) the relative skill of those in the art, and (8) the breadth of the claims.

The instant claims are directed to labeling a molecule with a second harmonic-active moiety and detecting the labeled molecule at the interface using a surface selective technique. The specification on page 16, lines 24-26 disclose the use of amine-specific dyes and sulfhydryl-specific dyes for second-harmonic active moieties. However it does not disclose the use of all second-harmonic active moieties. Furthermore, second-harmonic active moieties are not well known in the art and thus one of ordinary skill in the art would have a low level of predictability in the art.

The working examples in the specification are limited to the use of two specific dyes (1) The sulfhydryl-specific dye 1-(2,3-epoxypropyl-4-(5-(4-methoxyphenyl oxazol-2-yl)pyridinium trifluoromethanesulfonate (PyMPO epoxide), and the amine-specific dye 1-(3-(succinimidyloxycarbonyl)benzyl)-4-(5-(4-methoxyphenyl) oxazol-2-yl) pyridinium bromide (PyMPO, SE). At best, the detection of the molecule can be determined only by using amine-specific dyes or sulfhydryl-specific dyes and not all second-harmonic active moieties. Such is not seen as sufficient to support the breath of the claims and one skilled in the art cannot practice the claimed invention without undue experimentation, because in order to select an appropriate second harmonic active moiety, one skilled in the art would have to have a high level of predictability, in order to successfully select a second-harmonic active moiety without undue experimentation.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 17-28 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 17-20 provide for the use of a second harmonic-active moiety, but, since the claim does not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.

Claims 17-20 are rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd.* v. *Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

Claim 21, line 27 the recitation "exposing" is vague. It is unclear if exposing means that the surface physically contacts the medium or if the surface is brought in close proximity to the medium.

Claim Rejections - 35 USC § 102

1. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

2. Claims 1-4, 7, 8, 12, 13, 21, 23, 27 and 28 are rejected under 35 U.S.C. 102(b) as being anticipated by Quinn et al (EP 0740156).

Quinn et al disclose the use of nonlinear optical methods of surface second-harmonic and sum-frequency generation to detect and quantify antibody-antigen interactions, polynucleotide hybridization and enzyme-substrate complexes (col 1, lines 7-11). Quinn et al disclose that antibodies, antigens, polynucleotides or enzymes are attached to a sensor surface (col 4, lines 1 and 2). Quinn et al disclose that a reporter molecule (label) which possess a molecular excitation close to 2f may be attached by covalent or other means to the antibody, antigen, or enzyme thereby producing a

condition of resonance enhancement (col 2, lines 46-57). Quinn et al disclose that the surface is into contact with a solution which may contain the complementary species. Formation of a complex between the complementary species will result in a modification of the surface nonlinear optical properties. Measurement of the magnitude, angular dependence or any other parameter dependent on changes of nonlinear optical properties such as surface second-harmonic generation can be used to determine the amount of complex formation at the surface (col 4, lines 39-49).

Claim Rejections - 35 USC § 103

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

4. Claims 5, 24 and 25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Quinn et al (EP 0740156) in view of Mattingly et al (US Patent 5,145,790).

See above for teachings of Quinn et al.

Quinn et al differ from the instant invention in failing to disclose the molecule being a pollutant.

Mattingly et al disclose specific binding reagents, such as antibodies, for detecting the presence or amount of polychlorinated biphenyls in a test sample (col 2, lines 10-34).

It would have been obvious to one of ordinary skill in the art to use the polychlorinated biphenyl specific antibodies taught by Mattingly et al in the method of Quinn et al because Quinn et al is generic with respect to the analyte that is to be detected and one would use the appropriate reagent, i.e. antibody to detect the desired analyte, in this case polychlorinated biphenyls.

5. Claims 6, 11 and 22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Quinn et al (EP 0740156) in view of Marshall et al (US Patent 5,236,826).

See above for teachings of Quinn et al.

Quinn et al differ from the instant invention in failing to disclose detecting analyte molecule on a surface of a nanoparticle or polymer bead. Quinn et al also fail to disclose a plurality of individual second harmonic-active labels bound together to increase the overall nonlinear susceptibility of the second harmonic-active moiety.

Marshall et al disclose the use beads or particles which have bound to their surface a molecule. These particles increase the surface area of the solid support and the use of these particles increase favorable reaction kinetics through Brownian motion, thereby establishing equilibrium faster than a system with less available surface for binding.

It would have been obvious to one of ordinary skill in the art to incorporate the use of particles as taught by Marshall et al into the method of Quinn et al because Marshall et al shows that these particles increase the surface area of the solid support and the use of these particles increase favorable reaction kinetics through Brownian

motion, thereby establishing equilibrium faster than a system with less available surface for binding.

With respect to the plurality of individual second harmonic-active labels bound together in a fixed and determinate orientation with respect to each other so as to increase the overall nonlinear susceptibility of the second harmonic-active moiety as recited in the instant claims, the optimum overall nonlinear susceptibility of the second harmonic-active moiety can be determined by routine experimentation and thus would have been obvious to one of ordinary skill in the art. Further, it has long been settled to be no more than routine experimentation for one of ordinary skill in the art to discover an optimum value of a result effective variable. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum of workable ranges by routine experimentation." Application of Aller, 220 F.2d 454,456, 105 USPQ 233, 235-236 (C.C.P.A. 1955). "No invention is involved in discovering optimum ranges of a process by routine experimentation ." Id. At 458,105 USPQ at 236-237. The "discovery of an optimum value of a result effective variable in a known process is ordinarily within the skill of the art." Application of Boesch, 617 F.2d 272,276, 205 USPQ 215, 218-219 (C.C.P.A. 1980).

6. Claim 9 is rejected under 35 U.S.C. 103(a) as being unpatentable over Quinn et al in view of Buechler et al (US Patent 6,194,222).

See above for teachings of Quinn et al.

Quinn et al differ from the instant invention in failing to disclose the non-specific interaction being an electrostatic interaction.

Buechler et al disclose labels which are bound to the molecule by electrostatic interactions (col 21, lines 1-10). These interactions allow for an immunoassay system that is simple, rapid and reliable. Reliability in an immunoassay system is critical for the accurate measurement of the analyte (col 1, lines 40-43).

It would have been obvious to one of ordinary skill in the art to incorporate electrostatic interactions as taught by Buechler et al for the binding of the second harmonic-active moiety to the molecule of Quinn et al because Buechler et al shows that these interactions allow for an immunoassay system that is simple, rapid and reliable.

7. Claim 10 is rejected under 35 U.S.C. 103(a) as being unpatentable over Quinn et al (EP 0740156) in view of Wang et al (US Patent 5,696,157).

See above for teachings of Quinn et al.

Quinn et al differ from the instant invention in failing to disclose that the second harmonic-active moiety is specific for an amine group.

Wang et al disclose labels which are specific for amine groups. These amine-reactive dyes are of particular relevance as they are commonly used to label proteins and polypeptides (col 13, lines 50-63). These labels are able to preferentially label a specific ingredient or component in a sample and enable the researcher to determine the presence, quantity or location of that specific ingredient or component (col 1, lines 11-19).

It would have been obvious to one of ordinary skill in the art to substitute the label as taught by Wang et al for the label of Quinn et al because Wang et al shows that

these amine labels are of particular relevance as they are commonly used to label proteins and polypeptide and that these labels are able to preferentially label a specific ingredient or component in a sample and enable the researcher to determine the presence, quantity or location of that specific ingredient or component.

Furthermore, since the amine-specific dyes of Wang et al is within the chemical class as disclosed in the specification on page 16, line 24 (amine-specific dyes), it is considered that the amine-specific dye of Wang et al would be a second-harmonic active moiety.

8. Claims 14 and 16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Quinn et al (EP 0740156) in view of Eisenthal et al (Photophysics of liquid Interfaces by Second Harmonic Spectroscopy, J.Phys. Chem 1996, 100, vol. 31, 12997-13006).

See above for teachings of Quinn et al.

Quinn et al differ from the instant invention in failing to disclose an air-water interface and a water-glass interface.

Eisenthal et al disclose the investigation of interface properties using second-harmonic spectroscopy. Eisenthal et al disclose studies of molecules at the silica/water interface and at the air/water interface. The study of molecules at these interfaces provide new information and insights into equilibrium and dynamic processes occurring at interfaces. These liquid interfaces not only are of great scientific interest but also directly impact many areas of medicine and technology (page 12998)

It would have been obvious to one of ordinary skill in the art to incorporate the interfaces as taught by Eisenthal et al into the method of Quinn et al because Eisenthal et al show that the study of molecules at these interfaces provide new information and insights into equilibrium and dynamic processes occurring at interfaces and that these liquid interfaces not only are of great scientific interest but also directly impact many areas of medicine and technology.

9. Claim 15 is rejected under 35 U.S.C. 103(a) as being unpatentable over Quinn et al (EP 0740156) in view of Conboy et al (J. Chem. 1994, 98, 9688-9692).

See above for teachings of Quinn et al.

Quinn et al differ from the instant invention in failing to teach an oil-water interface.

Conboy et al disclose the investigation of oil-water interfaces. The study of this interface demonstrates the utility of using second harmonic generation to measure properties of the oil-water interface in the absence of any optical resonances and expand the range of systems which can be examined by second harmonic generation (abstract and introduction). Conboy et al also disclose that there is a high interest in the characterization of oil-water interfaces because of the central role which they play in many areas of chemistry, physics, and biology.

It would have been obvious to one of ordinary skill in the art to incorporate the oil-water interface as taught by Conboy et al into the method of Quinn et al because Conboy et al shows that the study of this interface demonstrates the utility of using second harmonic generation to measure properties of oil-water interface in the absence

of any optical resonances and expand the range of systems which can be examined by second harmonic generation. Conboy et al also that there is a high interest in the characterization of oil-water interfaces because of the central role which they play in may areas of chemistry, physics, and biology.

10. Claim 26 is rejected under 35 U.S.C. 103(a) as being unpatentable over Quinn et al (EP 0740156) in view of Tadano et al (US Patent 5,962,248).

See above for teachings of Quinn et al.

Quinn et al differ from the instant invention in failing to disclose the molecule being a chloride ion.

Tadano et al disclose a reagent for detecting chloride ions in a sample (col 1, line 66 – col 2, line 10).

It would have been obvious to one of ordinary skill in the art to use the enzyme substrate specific for chloride ions taught by Tadano et al in the method of Quinn et al because Quinn et al is generic with respect to the analyte that is to be detected and one would use the appropriate reagent, i.e. enzyme substrate to detect the desired analyte, in this case chloride ion.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gary W. Counts whose telephone number is (703) 305-1444. The examiner can normally be reached on M-F 8:00 - 4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on (703) 305-3399. The fax phone numbers for

the organization where this application or proceeding is assigned are (703)308-4242 for regular communications and (703)3084242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Gary W. Counts
Examiner
Art Unit 1641
February 5, 2002

CHRISTOPHER L. CHIN
PRIMARY EXAMINER
GROUP ~~1800~~ 1641